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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,724	11/07/2001	Michael N. Gould	960296.97711	7402

27114 7590 04/08/2004

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EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,724	GOULD ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004 and 29 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the supplemental response filed 2/2/04 wherein Applicant corrected a sentence that was submitted in a response filed 12/20/03.

Note: Claims 17-33 are pending.

RESPONSE TO APPLICANT'S ARGUMENTS/AMENDMENT

2. The Applicant's arguments filed 12/29/03 and 2/2/04 to the rejection of claims 17-33 made by the Examiner under 35 USC 103 and/or double patenting have been fully considered and deemed persuasive-in-part for the reasons set forth below.

Double Patenting Rejections

The provisional rejection of claims 17-33 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending application numbers 09/465,300; 09/466,582; 09/599,364; 09/281,209; and 09/948,807 are MAINTAINED for reasons of record in the office action mailed 7/22/02.

Note: It is once again noted that Applicant intends to rebut the double patenting rejections once all other outstanding rejections are withdrawn.

103 Rejections

The 103 rejections are WITHDRAWN for reasons of record in Applicant's response.

NEW GROUNDS OF REJECTIONS

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 17-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 09/878,797. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of sensitizing tumor cells. The claims differ in that the instant

claims are directed to chemotherapy whereas the claims of 09/878,797 read on a method of sensitizing cells to a chemotherapeutic agent. It would have been obvious to one of ordinary skill that if tumor cells are sensitized to radiation and chemotherapeutic agents, then they would be sensitive to chemotherapy because chemotherapeutic agents are used for chemotherapy.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

112 First Paragraph Rejection

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 26-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cytokines, does not reasonably provide enablement for all immunomodulatory agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level

of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed to a method of sensitizing tumor cells to immunomodulatory agents whereon the tumor cells are treated with an immunomodulatory agent.

(2) State of the prior art

The references do not indicate which specific immunomodulatory agents or class(es) of agents that are useful with the claimed invention..

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. Independent claim 26 encompasses a vast number of possible immunomodulatory agents. Applicant's specification does not enable the public to make or use such a vast number of possible agents.

(4) Level of predictability in the art

The art pertaining to the immunomodulatory agents is highly unpredictable. Determining the various types of immunomodulatory agents or class(es) of agents requires various experimental procedures and without guidance that is applicable to all tumor cells, there would be little predictability in performing the claimed invention.

Hence, there is little predictability in performing the claimed invention, absent some guidance, since not all immunomodulatory agent have the same mode of operation.

(5) Amount of direction and guidance provided by the inventor

Independent claim 26 encompasses a vast number of immunomodulatory agents. Applicant's limited guidance does not enable the public to prepare such a numerous amount of agents. There is no directional guidance for immunomodulatory agents other than cytokines in the instant application. Hence, there is no enablement for all possible permutations and combinations of the immunomodulatory agents.

(6) Existence of working examples

Independent claim 26 encompasses a vast number of immunomodulatory agents. Applicant's limited working examples do not enable the public to prepare such a numerous amount of agents. While Applicant's claims encompass a plethora of possible immunomodulatory agents, the specification provides support only for cytokines.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible immunomodulatory agents known to exist.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue

experimentation. Furthermore, based on the unpredictable nature of the invention, the state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

112 Second Paragraph Rejection

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26-32: The claims as written are ambiguous because one cannot readily ascertain what is being claimed. Specifically, the claims as written read on a multitude of possible immunomodulatory agents. However, one of ordinary skill in the art would not be able to ascertain what agent(s) Applicant is claiming that are compatible with the instant invention. Applicant is respectfully requested to clarify the claim in order that one may determine what is being claimed.

103 Rejections

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 17-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Myers et al (US Patent No. 5,602,184) in view of Gould et al (US Patent No. 5,587,402).

Myers et al disclose a method of treating cancer by administering and effective amount of a terpene selected form a cyclic monoterpene, a non-cyclic monoterpene, a non-cyclic sesquiterpene, and a non-cyclic diterpene. Possible monoterpenes include limonene, beta myrcene, and citral. In addition, Myers disclose a method of sensitizing cancer to radiation by administer and effective amount of a terpene (see entire document, especially, abstract; column 2, lines 1-5; column 4, line 11 through column 5, line 15; column 9, lines 1-13; column 10, lines 19-24). In column 12, Example 3, the effect of limonene on radiation sensitivity on tumor cells is disclosed. Myers et al fail to disclose addition monoterpenes (i.e., perillyl alcohol) which may be used with their invention. In addition, the reference fails to disclose specific chemotherapeutic agents and cytokines useful with their invention.

Gould et al disclose the regression of mammalian cell tumors wherein perillyl alcohol is administered to a subject (see entire document, especially, abstract). In addition Gould et al disclose that various monoterpenes such as limonene, perillyl alcohol, sobrerol, myrcene, pinene, cavone, terpineol, and uroterpenol (see column 4, Table 1) were analyzed for their ability to inhibit isoprenylation in cells. The effects of dietary perillyl alcohol on tumor regression and inhibition in rats were studied (columns 5-6, lines 14-68 and 1-68, respectively). In column 7, lines 35-68, in vivo experiments were conducted using perillyl alcohol in subjects with leukemia. In column 8, lin3es 33-

58, experiments were conducted with perillyl alcohol and limonene. Later, IL-3 was added. It should also be noted that Gould et al disclose the use of cytokines such as alpha interferon or interleukin-3 in their leukemia experiments (column 7, lines 56 through column 8, line 58).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Myers et al using the teachings of Gould et al and list other various monoterpenes because both references are directed to monoterpenes which interact with tumor cells to result in tumor growth regression. In addition, Gould et al disclose that the monoterpenes themselves are chemotherapeutic agent candidates and the use of cytokines. Hence, a skilled practitioner in the art would be motivated to use the monoterpenes in combination with the cytokines or as chemotherapeutic agents in the method of sensitizing tumor cells as set forth by Myers et al. Also, a skilled practitioner in the art would be motivated to seek any possible chemotherapeutic agent for use with the invention of Myers et al because the document discloses that the purpose of adding the monoterpenes/sesquiterpenes is to sensitize tumor cells to chemotherapy. Since, both documents are directed to the used of monoterpenes with tumor cells, the references may be considered to be within the same field of endeavor. Thus, the references are combinable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. L. Jones
Primary Examiner
Art Unit 1616

April 5, 2004